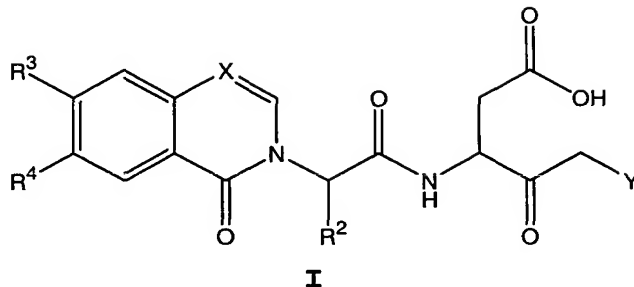


We claim:

1. A compound of formula **I**:



X is CH or N;

Y is halo, trifluorophenoxy, or tetrafluorophenoxy;

R<sup>2</sup> is C<sub>1-6</sub> straight chained or branched alkyl;

R<sup>3</sup> is hydrogen, halo, OCF<sub>3</sub>, CN, or CF<sub>3</sub>; and

R<sup>4</sup> is hydrogen, halo, OCF<sub>3</sub>, SR, CN, CF<sub>3</sub>, Ar, or T-Ar;

wherein:

T is O or S;

R is a C<sub>1-6</sub> straight chained or branched alkyl;

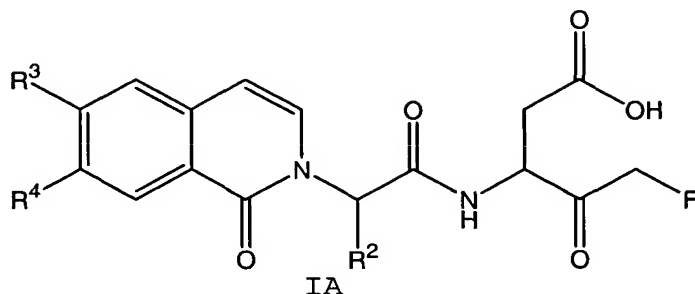
Ar is a phenyl ring optionally substituted with 1-3 groups selected from halo, CH<sub>3</sub>, CF<sub>3</sub>, CN, OMe, OCF<sub>3</sub>, and NR<sup>5</sup>R<sup>6</sup>; and

R<sup>5</sup> and R<sup>6</sup> each is independently H or C<sub>1-6</sub> straight chained or branched alkyl, or R<sup>5</sup> and R<sup>6</sup>, taken together, form a 5-7 membered ring optionally containing up to 3 heteroatoms selected from O, S, NH, and N(C<sub>1-6</sub>-straight chained or branched alkyl); provided that when Y is halo, then both, R<sup>3</sup> and R<sup>4</sup>, are not simultaneously hydrogen.

2. The compound according to claim 1, wherein R<sup>2</sup> is ethyl, n-propyl, or isopropyl.

3. The compound according to claim 2, wherein Y is F, trifluorophenoxy, or tetrafluorophenoxy.

4. The compound according to claim 1, having formula IA:



wherein:

$R^2$  is ethyl, n-propyl, or isopropyl; and

$R^3$  and  $R^4$  are each independently hydrogen, halo,  $OCF_3$ , CN,  $CF_3$  or Ar, provided that both,  $R^3$  and  $R^4$ , are not simultaneously hydrogen.

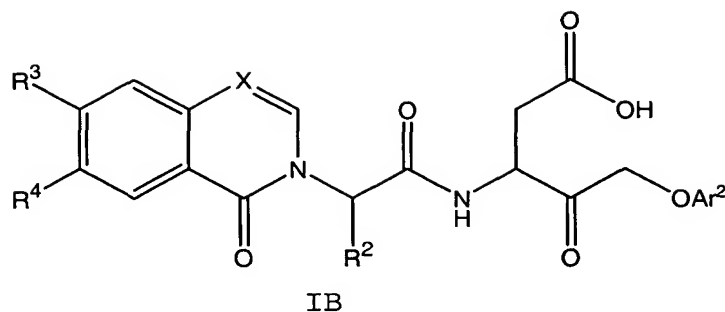
5. The compound according to claim 4, wherein  $R^2$  is ethyl.

6. The compound according to claim 4, wherein  $R^3$  is hydrogen.

7. The compound according to claim 4 or claim 5, wherein  $R^3$  is H, and  $R^4$  is F, Cl, CN, Ar, or  $CF_3$ .

8. The compound according to claim 7, wherein  $R^4$  is Cl or  $CF_3$ .

9. The compound according to claim 1, having the formula IB:



wherein:

X is CH or N;

R<sup>2</sup> is ethyl, n-propyl, or isopropyl;

R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen, halo, OCF<sub>3</sub>, CN, or CF<sub>3</sub>; and

Ar<sup>2</sup> is trifluorophenyl or tetrafluorophenyl.

10. The compound according to claim 9, wherein Ar<sup>2</sup> is 2,3,5,6-tetrafluorophenyl.

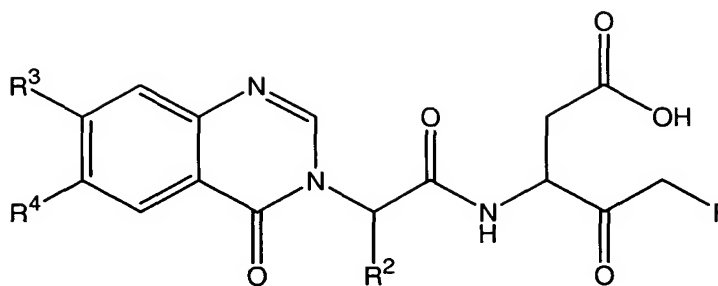
11. The compound according to claim 9, wherein R<sup>2</sup> is ethyl.

12. The compound according to claim 9, wherein X is CH.

13. The compound according to claim 12, wherein R<sup>4</sup> is Cl or CF<sub>3</sub>.

14. The compound according to any one of claims 9-12, wherein R<sup>3</sup> is H, and R<sup>4</sup> is F, Cl, or CF<sub>3</sub>.

15. The compound according to claim 1, having formula IC:



IC

wherein:

$R^2$  is ethyl, n-propyl, or isopropyl;

$R^3$  is hydrogen, halo,  $OCF_3$ , CN, or  $CF_3$ ;

$R^4$  is halo,  $OCF_3$ , CN,  $CF_3$ , SR, or T-Ar;

T is O or S;

R is a  $C_{1-6}$  straight chained or branched alkyl;

Ar is a phenyl ring optionally substituted with 1-3 groups selected from halo,  $CH_3$ ,  $CF_3$ , CN, OMe,  $OCF_3$ , and  $NR^5R^6$ ; and

$R^5$  and  $R^6$  each is independently H or  $C_{1-6}$  straight chained or branched alkyl, or  $R^5$  and  $R^6$ , taken together, form a 5-7 membered ring optionally containing up to 3 heteroatoms selected from O, S, NH, and N( $C_{1-6}$ -straight chained or branched alkyl).

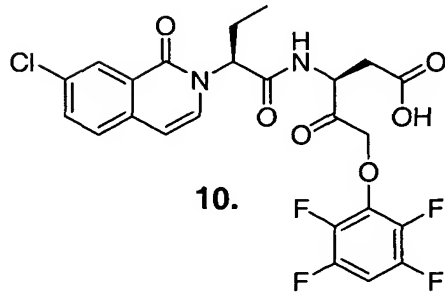
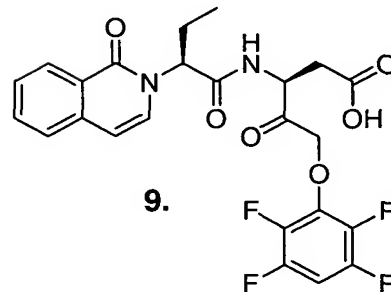
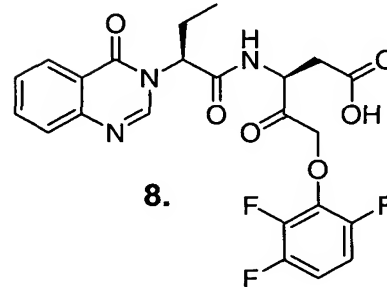
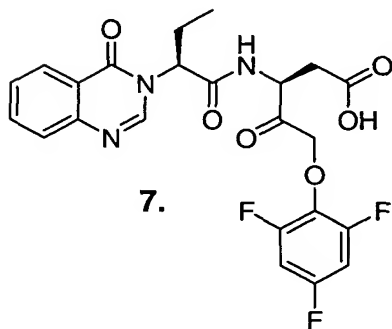
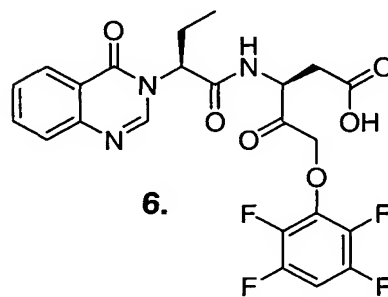
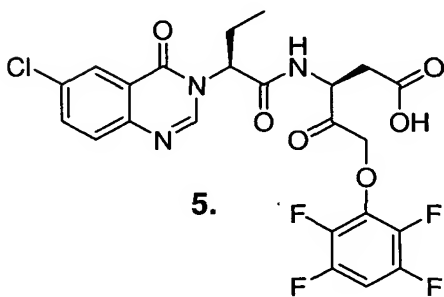
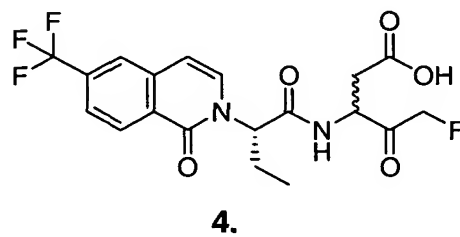
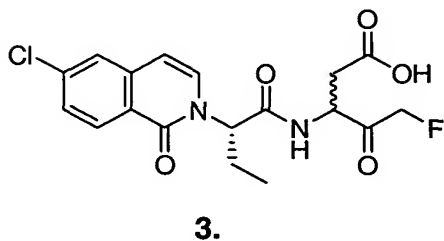
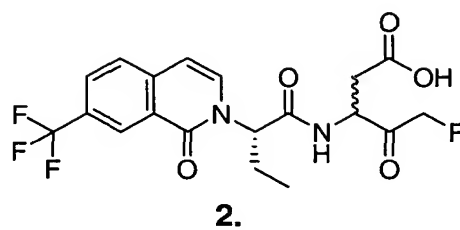
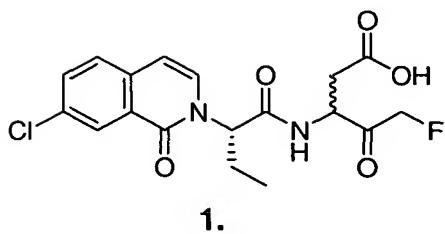
16. The compound according to claim 15, wherein  $R^2$  is ethyl.

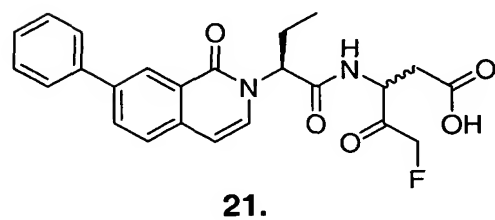
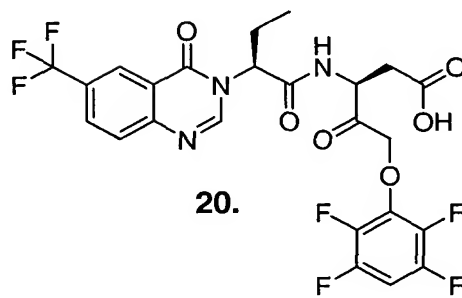
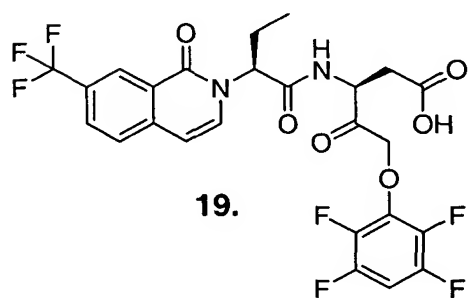
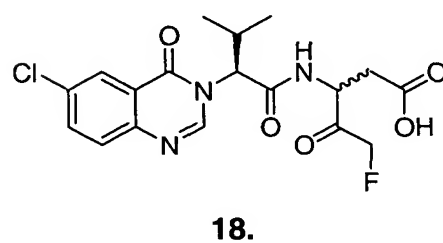
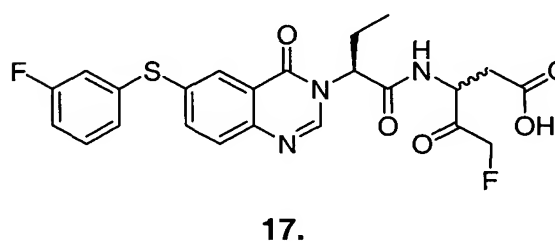
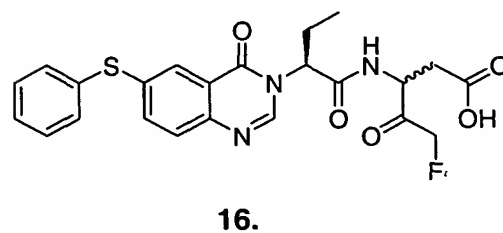
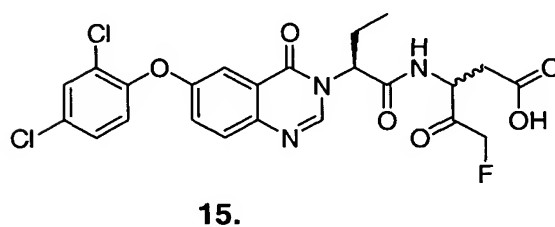
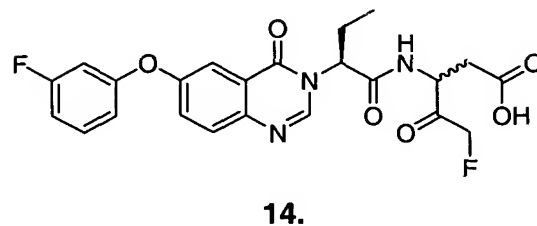
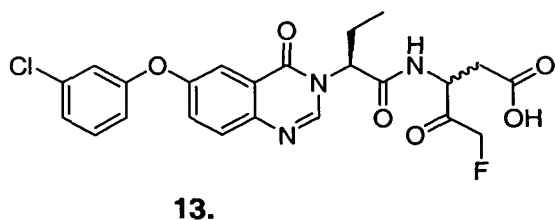
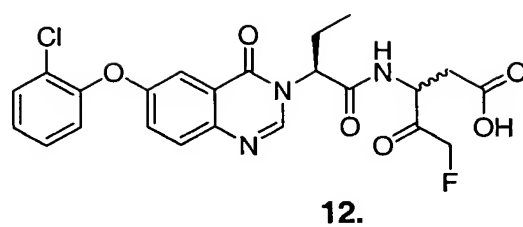
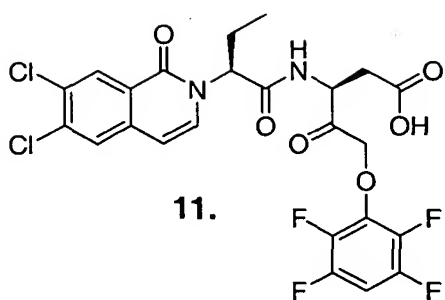
17. The compound according to claim 15, wherein  $R^3$  is hydrogen.

18. The compound according to claim 15, wherein T is O.

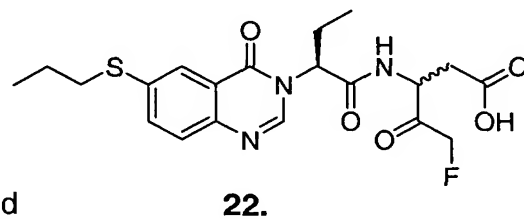
19. The compound according to any one of claims 15-18, wherein  $R^4$  is T-Ar.

20. The compound of claim 1, selected from:





and



21. A pharmaceutical composition comprising:

- a) a compound according to claim 1; and
- b) a pharmaceutically acceptable carrier, adjuvant or vehicle.

22. A method for treating a disease in a patient, wherein said disease is selected from an IL-1 mediated disease, an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a destructive bone disorder, a proliferative disorder, an infectious disease, a degenerative disease, a disease associated with cell death, an excess dietary alcohol intake disease, a viral mediated disease, retinal disorders, uveitis, inflammatory peritonitis, osteoarthritis, pancreatitis, asthma, adult respiratory distress syndrome, glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, inflammatory bowel disease, Crohn's disease, psoriasis, atopic dermatitis, scarring, graft vs host disease, organ transplant rejection, organ apoptosis after burn injury, osteoporosis, leukemias and related disorders, myelodysplastic syndrome, multiple myeloma-related bone disorder, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, haemorrhagic shock, sepsis, septic shock, burns, Shigellosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Kennedy's disease, prion disease, cerebral ischemia, epilepsy, myocardial ischemia, acute and chronic heart disease, myocardial infarction, congestive heart failure,

atherosclerosis, coronary artery bypass graft, spinal muscular atrophy, amyotrophic lateral sclerosis, multiple sclerosis, HIV-related encephalitis, aging, alopecia, neurological damage due to stroke, ulcerative colitis, traumatic brain injury, spinal cord injury, hepatitis-B, hepatitis-C, hepatitis-G, yellow fever, dengue fever, or Japanese encephalitis, various forms of liver disease, renal disease, polycystic kidney disease, H. pylori-associated gastric and duodenal ulcer disease, HIV infection, tuberculosis, meningitis, organ failure, treating complications associated with coronary artery bypass grafts, and an immunotherapy for the treatment of various forms of cancer;

said method comprising the step of administering to said patient a pharmaceutical composition according to claim 21.

23. The method according to claim 22, wherein the disease is an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a destructive bone disorder, a proliferative disorder, an infectious disease, a degenerative disease, a disease associated with cell death, an excess dietary alcohol intake disease, a viral mediated disease, inflammatory peritonitis, glomerulonephritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, scarring, graft vs host disease, organ transplant rejection, organ apoptosis after burn injury, osteoporosis, leukemias and related disorders, myelodysplastic syndrome, metastatic melanoma, haemorrhagic shock, sepsis, septic shock, burns, Shigellosis, Alzheimer's disease, Parkinson's



disease, Huntington's disease, Kennedy's disease, prion disease, cerebral ischemia, epilepsy, myocardial ischemia, acute and chronic heart disease, myocardial infarction, congestive heart failure, atherosclerosis, coronary artery bypass graft, spinal muscular atrophy, amyotrophic lateral sclerosis, multiple sclerosis, HIV-related encephalitis, aging, alopecia, neurological damage due to stroke, traumatic brain injury, spinal chord injury, hepatitis-B, hepatitis-C, hepatitis-G, various forms of liver disease, renal disease, polycystic kidney disease, H. pylori-associated gastric and duodenal ulcer disease, HIV infection, tuberculosis, meningitis, treating complications associated with coronary artery bypass grafts, and an immunotherapy for the treatment of various forms of cancer.

24. A method for inhibiting a caspase-mediated function in a patient comprising the step of administering to said patient a pharmaceutical composition according to claim 21.

25. The method according to claim 24, for decreasing IGIF or IFN- $\gamma$  production in a patient.

26. The method according to claim 23, wherein said disease is complications associated with coronary artery bypass grafts.

27. A method of preserving cells, said method comprising the step of bathing the cells in a solution of the compound according to claim 1 or a pharmaceutically acceptable derivative thereof.

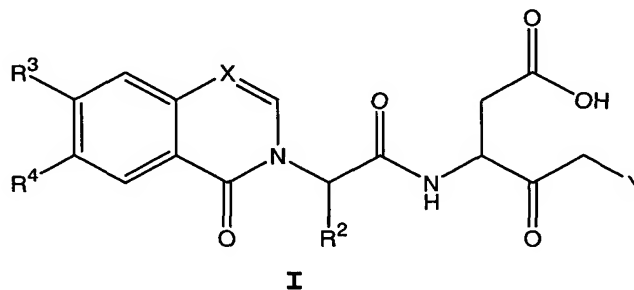
28. The method according to claim 27, wherein said cells are in:

- a) an organ intended for transplant; or
- b) a blood product.

29. A method of treating cancer using immunotherapy, wherein said immunotherapy comprises as a component thereof a compound according to claim 1.

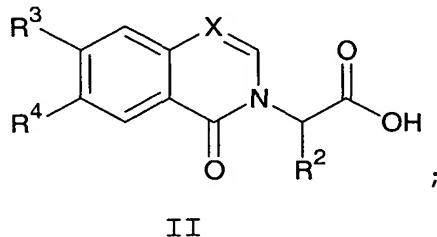
30. The method according to claim 23 wherein said composition comprises an additional therapeutic agent.

31. A method of preparing a compound of formula I,

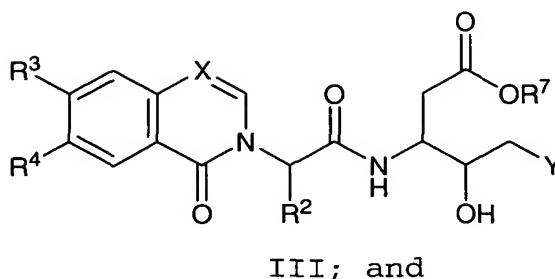
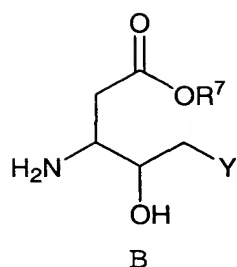


said method comprising:

reacting an acid or acid derivative of formula II,



with an amino alcohol of formula B, to provide a compound of formula III,



converting intermediate III to compound I, wherein;

X is CH or N;

Y is halo, trifluorophenoxy, or tetrafluorophenoxy;

R<sup>2</sup> is a C<sub>1-6</sub> straight chained or branched alkyl;

R<sup>3</sup> is hydrogen, halo, OCF<sub>3</sub>, CN, or CF<sub>3</sub>; and

R<sup>4</sup> is hydrogen, halo, OCF<sub>3</sub>, SR, CN, CF<sub>3</sub>, Ar, or T-Ar;

wherein:

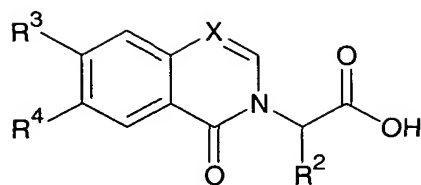
T is O or S;

R is a C<sub>1-6</sub> straight chained or branched alkyl;

Ar is a phenyl ring optionally substituted with 1-3 groups selected from halo, CH<sub>3</sub>, CF<sub>3</sub>, CN, OMe, OCF<sub>3</sub>, and NR<sup>5</sup>R<sup>6</sup>;

R<sup>5</sup> and R<sup>6</sup> each is independently H or C<sub>1-6</sub> straight chained or branched alkyl, or R<sup>5</sup> and R<sup>6</sup>, taken together, form a 5-7 membered ring optionally containing up to 3 heteroatoms selected from O, S, NH, and N(C<sub>1-6</sub>-straight chained or branched alkyl); and R<sup>7</sup> is a suitable protecting group; provided that when Y is halo, then both, R<sup>3</sup> and R<sup>4</sup>, are not simultaneously hydrogen.

32. A compound of formula IIA:



IIA

wherein;

X is CH or N;

R<sup>2</sup> is a C<sub>1-6</sub> straight chained or branched alkyl;

R<sup>3</sup> is hydrogen, halo, OCF<sub>3</sub>, CN, or CF<sub>3</sub>; and

R<sup>4</sup> is hydrogen, halo, OCF<sub>3</sub>, SR, CN, CF<sub>3</sub>, Ar, or T-Ar;

wherein:

T is O or S;

R is a C<sub>1-6</sub> straight chained or branched alkyl;

Ar is a phenyl ring optionally substituted with 1-3 groups selected from halo, CH<sub>3</sub>, CF<sub>3</sub>, CN, OMe, OCF<sub>3</sub>, and NR<sup>5</sup>R<sup>6</sup>; and

R<sup>5</sup> and R<sup>6</sup> each is independently H or C<sub>1-6</sub> straight chained or branched alkyl, or R<sup>5</sup> and R<sup>6</sup>, taken together, form a 5-7 membered ring optionally containing up to 3 heteroatoms selected from O, S, NH, and N(C<sub>1-6</sub>-straight chained or branched alkyl).

33. The compound according to claim 31 or 32 wherein R<sup>2</sup> is ethyl or isopropyl.